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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,342	03/06/2002	Kevin Burke	7601/80250	1549

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,342	BURKE ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-16 have been canceled. Newly presented claims 17-36 are at issue and are present for examination.

Applicants' arguments filed on 9/17/04, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 17-19 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not contain any disclosure of methods of preparing of any *Corynebacterium glutamicum* in which the activity of the endogenous poxB gene of SEQ ID NO:4 has been reduced or eliminated. The genus of *Corynebacterium glutamicum* bacteria in which the activity of the poxB of SEQ ID NO:5 has been reduced or eliminated is a large variable genus encompassing many different structural modifications of the bacteria. The specification discloses only a single species of the claimed genus (i.e., *Corynebacterium glutamicum*

DSM5715:pCr.1poxBint/pEC-T18mob2zwf) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicants appear to believe that the amendments of the claims to limit the claimed methods to the use of *Corynebacterium glutamicum* which overexpress a ZWF protein of SEQ ID NO:8 or SEQ ID NO:10 and having decreased or eliminated activity of the pyruvate oxidase of SEQ ID NO:5 to be sufficient to overcome the instant rejection. However, the instant rejection is maintained for all of current claims 17-19 and 24-29 as these claims recite the use of *Corynebacterium glutamicum* bacteria in which the activity of the poxB of SEQ ID NO:5 has been reduced or eliminated by any method. The activity of a particular protein within any microorganism can be reduced or eliminated by many different means including mutagenesis or disruption of the endogenous gene or of other endogenous proteins which regulate the desired protein, by antisense expression, by production of a one or more inhibitors of the protein, and by alteration of the regulatory regions of the endogenous gene or of other endogenous proteins which regulate

the desired protein or its expression. Each of these methods require different structural modifications of the bacteria. However the specification describes only a single means of reducing or eliminating the activity of the pyruvate oxidase of SEQ ID NO:5 in *Corynebacterium glutamicum*.

Claims 17-19 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of making an amino acid using *Corynebacterium glutamicum* containing an inactivating deletion in the endogenous poxB gene of SEQ ID NO:4 and transformed with a nucleic acid encoding the zwf protein of SEQ ID NO:8 or 10, does not reasonably provide enablement for methods of making any amino acid using a *Corynebacterium glutamicum* in which the zwf protein of SEQ ID NO:8 or 10 is overexpressed and the activity of the pyruvate oxidase of SEQ ID NO:5 has been reduced or eliminated by any means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicants argue that the Examiner's arguments insofar as they allege that the claims are not enabled because the specification does not teach all methods for decreasing the activity of the poxB gene are incorrect. Applicants argue that

although such allegations would be appropriate if Applicants were claiming methods for modifying the activity of these genes, they are not appropriate for the claims that are presently pending. The pending claims are directed to methods for producing amino acids using bacteria that have been engineered to have increased zwf gene activity and decreased poxB gene activity. Applicants argue that enablement of this invention only requires that Applicants provide one method by which the invention can be made and used and this has clearly been done in the specification. Any other method for amplifying zwf or decreasing poxB will produce a bacterium that is equally useful in the invention as claimed. It is the bacteria, not the method by which they are made, that is important to the invention. Applicants argument is not persuasive because enablement for a method of using a genus of bacteria as is encompassed by the instant claims clearly requires that the specification teach how to make the genus of bacteria which must be used. While the specification teaches one such bacterium and the specification and art clearly enables the skilled artisan to make other similar modifications of the coding region of SEQ ID NO:4 which would reduce or eliminate the enzymatic activity of the encoded enzyme, the specification and art do not enable the skilled artisan to make any *Corynebacterium glutamicum* in which the zwf

protein of SEQ ID NO:8 or 10 is overexpressed and the activity of the pyruvate oxidase of SEQ ID NO:5 has been reduced or eliminated. As such the specification has not enabled the skilled artisan to make and use the full scope of the methods claimed.

Claims 17-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunican et al. (WO 01/04322) in view of Möckel et al. (EP 1 096 013, see enclosed English equivalent document AU 200068075) and JP 09-244661.

Dunican et al. teach methods of making amino acids, in particular lysine and threonine, comprising fermentation of a *Corynebacterium glutamicum* which produces L-lysine, L-threonine, L-isoleucine, or L-tryptophan, in which the zwf gene (encoding a glucose-6-phosphate dehydrogenase subunit) of a Coryneform bacteria is overexpressed and the poxB gene of the bacterium is attenuated. Dunican et al. do not teach a zwf gene encoding SEQ ID NO:8 or 10 or a poxB gene encoding SEQ ID NO:5

JP 09-244661 teaches a Brevibacterium flavum zwf gene identical to SEQ ID NO:8.

Möckel et al. teach a *Corynebacterium glutamicum* poxB gene encoding the protein of SEQ ID NO:5, methods for the attenuation of the expression of this gene in *Corynebacterium glutamicum* by integration mutagenesis using the plasmid pCR2.1poxBint and

methods for making amino acids using the *Corynebacterium glutamicum* having the poxB gene attenuated therein.

Therefore, it would have been obvious to one of ordinary skill in the art to make a *Corynebacterium glutamicum* in which the zwf gene of JP 09-244661 is overexpressed and the poxB gene of the bacterium is attenuated as taught by Dunican et al. It would have been further obvious to use any of the specific *Corynebacterium glutamicum* strains listed by Dunican et al. on pages 6-7 as the strain to be modified and to then use these strains for the production of L-lysine, L-threonine, L-isoleucine, or L-tryptophan. Claims 18, 21, 26, and 31 specifically recite that the zwf gene used encodes SEQ ID NO:10. SEQ ID NO:10 differs from the gene of SEQ ID NO:8 disclosed in JP 09-244661 in the inclusion of 30 additional N-terminal amino acids. However, Dunican et al. teach that the natural N-terminus of the *Corynebacterium glutamicum zwf* gene has the sequence Xaa Xaa Xaa Xaa Xaa Pro Xaa Xaa Trp Xaa Asn Pro Leu Arq Asp and teach a *Corynebacterium glutamicum zwf* gene having this N-terminal amino acid sequence which includes a 29 amino acid N-terminal sequence following a GTG initiation codon and preceding an amino acid sequence identical to SEQ ID NO:8 except for a single substitution at amino acid 120 of SEQ ID NO:8. Thus the zwf gene of Dunican et al. encodes a protein identical to SEQ ID

NO:10 except for an N-terminal Val residue and a single amino acid substitution at amino acid 150 of SEQ ID NO:10. It would have been obvious to one of skill in the art to modify the amino terminal GTG codon of the zwf gene of Dunican et al. to an ATG codon, as ATG is well known in the art to be the most preferred initiation codon in bacteria. Furthermore, it would have been obvious to one of skill in the art that the amino acid at position 150 of the gene of Dunican et al. could be either alanine as in the zwf gene of Dunican et al. or threonine as in the zwf gene of JP 09-244661 as the proteins are otherwise identical. As such using a zwf gene of SEQ ID NO:10 would have been obvious to one of ordinary skill in the art.

It is noted that the Dunican et al. (WO 01/04322) and Möckel et al. (EP 1 096 013) references were published after the filing date of applicants parent application (09/531,269). However, the prior application does not support the current claims as it does not describe zwf genes encoding the proteins of SEQ ID NOS:8 and 10. Furthermore, the instant rejection was necessitated by applicants amendments of the claims to recite zwf genes encoding the proteins of SEQ ID NOS:8 and 10 and thus the finality of the instant action is proper.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS**

ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (571) 272-0937. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600